

Engineered matrices for control of lineage commitment in human pancreatic stem cells

Grant Award Details

Engineered matrices for control of lineage commitment in human pancreatic stem cells

Grant Type: Basic Biology V

Grant Number: RB5-07398

Project Objective: This award will determine if lineage differentiation in adult human pancreatic progenitor cells may be regulated by engineered ECMs in vitro. These artificial ECMs (aECMs) will be designed to facilitate production of glucose-sensitive cells for treatment of Type I diabetes.

Investigator:

Name:	David Tirrell
Institution:	California Institute of Technology
Type:	PI

Disease Focus: Diabetes, Metabolic Disorders

Cell Line Generation: Adult Stem Cell

Award Value: \$526,896

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 2

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Grant Application Details

Application Title: Engineered matrices for control of lineage commitment in human pancreatic stem cells

Public Abstract:

Patients with end-stage type 1 diabetes (T1D) can be effectively managed by allogeneic islet transplantation. However, a severe cadaveric organ shortage greatly limits use of this promising procedure. Stem cells have the potential to provide a solution to this bottleneck because of their ability to self-renew and differentiate into islet β -cells. Although progress has been made in coaxing human embryonic stem (ES) cells to differentiate into pancreatic progenitor-like cells in culture, there are safety concerns regarding ES cell-derived products because of their ability to form teratomas in vivo. In contrast, adult tissue cells lack teratoma potential. Our goal is to develop, for transplantation, insulin-expressing cells derived from adult human pancreatic progenitor-like cells. If successful, the proposed research will establish a new paradigm for the development of cell products derived from adult pancreata and enable important advances in cell replacement therapy for T1D. This research will allow human cadaveric adult pancreatic tissues, which are largely discarded after islet isolation, to be used to maximum efficiency in transplantation. Moreover, the results of these studies will be applicable to the treatment of end-stage type 2 diabetes patients, in whom islet β -cells are exhausted and dysfunctional.

Statement of Benefit to California:

In type 1 and some type 2 diabetic patients, the pancreatic β -cells, which secrete insulin in response to elevated glucose concentrations in the blood, are insufficient or dysfunctional. Insulin injection is the most common form of therapy to control diabetes. However, insulin injection cannot match the physiological response conferred by endogenous β -cells, and complications inevitably develop over time. Allogeneic islet transplantation is beneficial to those diabetic patients who have developed end-stage complications. However, it is estimated that fewer than 1% of Californians most in need of islet transplantation can benefit from the procedure because there is a severe shortage of human cadaveric pancreas organs. This dire situation has led to the search for alternative sources of β -cells for transplantation. If human adult pancreatic stem and progenitor cells can be coaxed to differentiate into β -like cells in culture, they would provide large numbers of cells for replacement therapy. This proposal addresses the important challenge of producing β -cells through differentiation of human pancreatic stem and progenitor cells, with the ultimate objective of developing new treatments for diabetic patients.

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